anomalous character of the symptoms could lead us to suspect their nature. Leroy gives as an example of the diagnostic difficulties in these cases of bronchial concretions the following case reported by M. Barth (*Bull. Soc. Méd. des Hôp.*, 1865, p. 9:

> A young woman had a very serious and obstinate bronchitis, though auscultation gave no signs of its being of a tuberculous character. At a certain period of the disease the expectoration became very considerable, and one morning a concretion as large as a grape-seed was spit up; a little later a second concretion was expectorated. After this the health was rapidly restored. The concretions were believed to have ulcerated their way through the bronchial walls from the lymphatic glands.

Without going into profitless speculation as to the origin of the calculus thrown off in the original case reported, the opinion was formed that the concretion had probably been latent in the bronchus for a long time, and that in some way it was disturbed and caused to act as an irritant, making a *locus minor resistenciæ,* and in the light of modern bacteriology the habitat of the body and its adjoining tissue became infected; hence the bronchitis, the pneumonia, the tissue necrosis, and the happy termination in the freeing and expelling of the body. In this case, previous to the onset of the attack of bronchitis, the man had been employed at some unusually heavy and arduous work, shovelling coal in a coal-lighter. The unaccustomed exertion entailed in the performance of such extremely heavy labor could perhaps have disturbed the quiescent concretion.

PROGRESSIVE MUSCULAR DYSTROPHY, WITH THE REPORT OF AN AUTOPSY.[1]

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MORE than twelve years have passed since one (Sachs) of the present writers discussed the subject of progressive muscular atrophy before the American Neurological Association. During this period innumerable contributions have appeared relating to the amyotrophies and the dystrophies, yet many of the same questions which puzzled us at that time remain unsolved. It is generally assumed that the amyotrophies can be easily differentiated—at least clinically—from the progressive primary myopathies; the spinal forms are developed late in life; there is in them no distinct hereditary influence; the wasting begins in the upper extremities, and rarely in the lower; hypertrophy is the exception, fibrillary twitchings the rule, while the electrical changes are more or less pronounced, often leading to a complete reaction of degeneration. Contrast with this the early onset of the myopathies, the distinct hereditary and family taint in the victim of this affliction in whom the first symptoms appear in the lower extremities and not in the upper; hypertrophy is the rule, fibrillary twitchings the exception, while the electrical conditions show no very marked departure from the normal.

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[1] Read before the New York Neurological Society, March 5, 1901.

The simplicity of this clinical scheme is disturbed by the fact that a sufficient number of cases of spinal muscular disease have been reported in adults as well as in children, showing a distinct family taint. Some hypertrophied muscular fibres have been made out in these same forms, and often the electrical changes have been noted to be very slight indeed; on the other hand, the fibrillary twitchings and the reaction of degeneration which have been thought to be thoroughly characteristic of the amyotrophies have also been noted in the cases of primary myopathy. In view of the difficulty of making a proper clinical differentiation, an opinion uttered five years ago may be repeated here, that "it is wiser to be guided by the general agreement of symptoms than by any one single symptom." But even this will not help us altogether out of the difficulty, for Friedel Pick, for instance, reported only lately a case which he had diagnosticated as a spinal form of progressive muscular atrophy, but on post-mortem examination not a single trace of spinal disease could be made out. Similar experiences have led Placzek to decide that, in view of the many difficulties besetting the differentiation between the various groups of progressive muscular atrophy, it would be wiser not to attempt to distinguish between them and to regard all of them as belonging to a single morbid entity. It is doubtful, however, whether it is necessary at the present moment to accept this extreme view.

Remembering, also, that it is uncertain whether the peroneal form of progressive muscular atrophy should be classified with the amyotrophies, or whether it is properly designated as a progressive neural atrophy, we are bound to admit that the clinical distinction between the various amyotrophies and dystrophies is not as firmly established as we could wish. As between a progressive neural atrophy and an amyotrophy, the neuron theory will help us to account for the lack of a sharp line of demarcation in the symptomatology, and will also help to explain the difference in the anatomical findings of the cases of progressive neural atrophy hitherto reported, some authors finding distinct changes in the spinal cord and others denying the existence of these, and maintaining that the peroneal form is due solely to a peripheral nerve lesion. There is, indeed, a strong possibility that in some instances the distal end of the neuron, and in others the central end, may be more distinctly diseased; the clinical manifestations of such lesions would, however, differ but very little. One would, nevertheless, be justified in looking for a marked differentiation between the primary myopathies and the amyotrophies, unless it could be shown that even in the myopathies it is the distal end of the neuron which is first affected. Such evidence has not been furnished in abundance, although a lady physician, Dr. Saccara-Tulbure, has claimed to have found distinct changes in the terminal endings of the nerves in the muscles in a case of pseudohypertrophy. She insists that, by methods which she employed, she could make out a distinct diminution of the tufts and fibres in the terminal muscular plates. It is a little unfortunate that the case in which she has found this was not an entirely typical case of pseudohypertrophy, although it was allied in all probability to the group of progressive dystrophies.

In former years much stress was laid upon the histological structure of the muscles in the two groups of cases, and we were inclined to believe that the simple examination of a piece of muscle removed during life or post-mortem would help to establish a positive diagnosis. In the muscles removed from dystrophic patients hypertrophied fibres were abundantly in evidence, or else fibres that had undergone simple atrophy. In amyotrophies hypertrophied fibres were not found, and there was a marked degeneration, not a simple atrophy, of the muscular tissue. But since that time it has been shown by a number of authors that hypertrophied fibres occur in purely spinal affections, in infantile spinal paralysis, and in syringomyelia, for instance; while, on the other hand, Hoffman maintained, with good reasons, that simple atrophy of the muscular fibre occurs in the spinal forms of progressive muscular atrophy. Moreover, the question is still open for discussion whether or not the gray matter of the cord is affected in the primary dystrophies, and, if affected, whether such changes are primary or secondary. Erb, Pick, Kahler, Heubner, and others have reported changes in the gray spinal matter in cases of primary dystrophy. Erb and Strümpell regard these changes as secondary, but in the case of Strümpell, Hoffman, whose authority in this matter could hardly be questioned, doubts whether the case upon which the argument was founded was a primary dystrophy at all. In the attempt to reconcile conflicting views, Erb has interjected the further proposition that all the progressive myopathies (whether or not there be anatomical evidence of central nervous disease) are of neuropathic origin and due to *functional* disturbance of the trophic centres, and that the results of such disturbance of the trophic centres would be evident first in the parts furthest removed from these centres, namely, in the muscular tissue.

It is difficult to prove or to deny the truth of such speculation, but it would seem to us that if purely functional changes are to account for such a wide-spread disease as is progressive myopathy some slight structural change might be made out in the gray matter of the spinal cord in patients who have survived for many years the onset of the disease. The first case, upon which we report in detail, will offer valuable evidence in this direction, and the value of it is increased by the fact that the latest staining methods and the best technique have been employed by Dr. Brooks in his examination of the nerves and muscular system. We propose to show by the records of this case that in a progressive muscular dystrophy, lasting over fifteen years, the anatomical findings in the spinal cord were practically negative. In this special case the disease began as a typical pseudohypertrophy, but as the boy was one of a family of three in whom the second brother developed a characteristic juvenile form of progressive muscular atrophy, and another brother also developed a muscular pseudohypertrophy, we may infer that the negative findings of this case have a special value with regard to all the forms of progressive muscular dystrophy.

The clinical history of the patient, J. K., cannot be given with fullest details, because, unfortunately, some of the earlier records of the case were not retained at the Montefiore Home, into which institution the boy was admitted on December 15, 1889. But the loss of the earlier records matters little, for the boy was under observation for a period of nearly eleven years at the home, and during these eleven years his condition changed but very little. He died of pneumonia March 15, 1900. At the time of his admission he was thirteen years of age; was born in Russia; his parents were alive and well at that time. A younger brother had suffered from a similar affliction. This boy was also transferred to the home, where he died in 1898 of cardiac disease. He presented the clinical symptoms of Erb's juvenile type. Unfortunately, no autopsy was obtained. A third brother has the ordinary form of pseudohypertrophy. His present condition is unknown to us. There was no history of any other taint in our patient's family.[1] Early in life J. K.'s parents noticed constant movements of the head and of the eyes. He was practically well until the age of ten years, when he had a fall and is said to have broken his left leg. He was confined to bed a few weeks, recovered from the injury, and could walk about until one year later, when he fell again, and for a second time is supposed to have broken his leg at the same point. He recovered from the second fall, but could not walk about as well as formerly. One year before admission, at the age of twelve years, he was stricken with typhoid fever; was confined to his bed for two weeks, and when he arose from his sick bed and attempted to walk his parents noticed that he could not get about. A few weeks after this he could not walk at all. The hypertrophied calves were very striking at the first examination, but they had not attracted the attention of the parents. Barring a slight progression in the atrophies of the muscles, the boy's condition changed so little that it may be summarized as follows: The head was large, undergoing constant rotary movements, congenital nystagmus, macroglossia, and thick speech, all of which may be taken as distinct stigmata of degeneration, as has been noted in other cases of pseudohypertrophy. His general intelligence was fair. He was instructed while at the Home, and became a very assiduous reader. There was a marked atrophy of all the muscles at the shoulder girdle, the upper arm and forearm, the muscles of the hand alone preserving anything like a normal configuration, but the grasp of the hand was almost *nil.* He presented typical "loose" shoulders. The deep spinal muscles were intensely atrophied and caused distortion of the spinal column and trunk. The thigh muscles were atrophied, the calves remaining large and tough to the very end, although they had become diminished in size during the last few years. Both feet were club-shaped and in extreme valgus position. The exact measurements are given in the pathological report, and mention of them is therefore omitted from this clinical statement. During the last five or six years of his life the boy was only able to use his facial muscles and to hold his head erect when sitting in a chair. He was totally unable to raise his head from the pillow or to perform a single movement of the trunk or of the limbs. He had to be lifted about, as it were, *en masse*, and was a dead weight in the truest sense of the term. With the few exceptions above noted, the entire muscular system was useless. The case was, therefore, an extreme illustration of a progressive muscular dystrophy of a pseudohypertrophic type. The reflexes were, of course, absent. In the earlier years there was some response to the faradic current, which disappeared as the atrophy increased. The vesical and rectal reflexes remained normal to the very end. The general health was good, and if it had not been for the onset of pneumonia the boy might have lived for many years.

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[1] The pictures of these three brothers will be found in Sachs' Nervous Diseases of Children, pp. 422, 423, 424.

Pathological Report. The necropsy was performed twenty-four hours after death.

"The body is that of a small male. It shows great general deformity, and is much smaller than normal for a subject of this age, being about the size usual in a boy of fourteen or fifteen years. The head is, however, of natural size, and consequently appears proportionately very large to the small and wasted trunk and extremities.

"The face is asymmetrical, the right side is puffy, flabby, and has a paretic appearance not unlike that seen in myxœdema; the left side is much more natural, and has a more intelligent look. There is a scanty, fine growth of brown beard and moustache. The left eye and eyebrow are elevated, and the pupils are dilated irregularly. The nose is broad, short, and the alæ nasi are very thick and heavy. The oral cavity is very broad. The teeth are irregularly placed and badly shaped. The tongue is large, broad, and very thick, though proportionately thin at the tip, which is somewhat deviated to the left. The ears are large and project well from the head. The Darwinian tubercles are, however, small. The general expression of the features is dull and passive, and somewhat simulates the facial aspect of acromegalia.

"The forehead slopes back sharply and the integument covering it shows several deep transverse folds. The entire head is vertically elongated, so that the occipital protuberance projects but a short distance posterior to the line of the neck. The scalp is covered with a thick growth of fine brown hair, darker in color than the hair on the face.

"The neck is small as compared to the head, but is about proportionate to the trunk. The sternocleidomastoid muscles are contracted, and the head is rotated slightly to the right.

"Both arms and forearms are small, and their musculature is soft and flabby as well as scant in amount. The hands are small, delicate, and well formed. The fingers are medium flexed. The entire upper extremities may be said to be generally atrophied, the condition being much less marked in the hands than elsewhere; it seems like a passive atrophy, the hands being probably less atrophied on account of their greater functional activity.

"The thorax is greatly deformed. The entire cage is deviated laterally to the left, so that the right side projects sharply forward, the lower border returning to jut out toward the right. This deformity is caused by a marked latero-posterior curvature of the spinal column, the greatest deviation of which is to the left.

"The curvature of the spinal column causes a compensatory deviation of the pelvis to the right, so that its median line lies about 6 cm. to the right of the axis of the thorax and in the line of the head and neck. The blade of the right iliac bone is also deflected to the left, so that its crest reaches beyond the median line of the pelvis. The left ilium is correspondingly but much less deviated.

"The external genitals are small, but are normally formed.

"The lower extremities are very short, even as compared to the thorax. Both are flexed at the knees, and when extended the right measures, from the great trochanter to the plantar surface of the arch, 71.5 cm., and the same measurement on the left gives 73 cm. The musculature of the lower extremities is scant, that of the left side being of somewhat greater volume than that of the right. The musculature of the thighs and buttocks is small in amount, but is unusually solid to palpation. The calves are of small volume; at the point of greatest diameter the left measures 27 cm. and the right 25 cm. The peculiarity of these muscles is the curious wood-like, inelastic impression which they give to the palpating hand; in this they contrast very markedly with the soft and flabby muscles (though equally atrophied) of the upper extremities and neck. The feet are inverted so that the plantar surfaces are almost parallel. Both tendo Achilles are so contracted by the retraction of the calf muscles that the toes are drawn nearly to the axis of the shanks. The feet are thickened laterally, but are short, very firm and solid, resisting pitting almost completely, although they have the appearance of being œdematous. The circumference of the right foot at the arch is 26.4 cm., and the same point on the left gives a diameter of 23.8 cm. The length of the left foot from the tip of the os calcis to the end of the great toe is 18 cm., and that of the right foot 17.2 cm. The relative atrophy of the calf muscles is very apparent when one compares these measurements with those of the calves. The toes are all sharply flexed as though from contracture of the plantar muscles and tendons.

"The thoracic musculature is very small in amount, but that of the abdomen is more abundant, and the muscles here are of more natural color and consistency, though they show in lesser degree the changes which are most extreme in the greatly wasted pectoral muscles in which muscle tissue has apparently been substituted by strands of fibrous-appearing tissue of unnatural firmness and inelasticity.

"The lungs are collapsed, permitting a large exposed præcordia.

"Both pleural cavities are free and normal.

"The pericardial sac contains 20 c.c. of clear, light-colored serum. The epicardium shows a few areas of opalescence, which are most numerous, thickest, and largest over the left ventricle. The left ventricle of the heart is widely distended, while the right ventricle is collapsed. The aorta has a diameter of 5 cm. just above the sinuses. The aortic valves are normal, but there is a relative insufficiency of the mitral segments. The valves of the right heart are normal throughout. Both auricles contain small post-mortem clots, but the ventricles are for the most part empty. The myocardium shows a great diffuse fibroid infiltration, which is most extensive in the wall of the left ventricle, where it is distinctly patchy in distribution. The intima of the aorta and the endocardium is slightly thickened in places, but hardly enough so to be considered a pathological state. The coronary arteries are normal in appearance. Weight of heart, thirteen ounces.

"The aortic arch throughout the ascending and transverse portion shows a moderate arterio-sclerosis, which is not, however, continued into the carotids or other large branches.

"The lungs are moderately congested. There are several calcified tubercles in both apices, and a few scattering tubercles throughout the substance of both lungs, but in every instance the tubercles are surrounded by a dense, usually calcified capsule, and all are apparently quiescent. The tip of the right lower lobe is involved in an extensive area of recent bronchopneumonia, and the bronchi distributed to this area are filled with a thick, yellowish pus.

"The tongue is very large. It measures from tip to the base of the epiglottis 14.5 cm., and is 7.6 cm. broad at its widest part. It is 3.6 cm. in thickness.

"The lymph nodules of the posterior dorsum are enlarged and moderately injected.

"The lymphatic tissue of the pharynx is generally hypertrophied It is otherwise normal.

"The thyroid gland is of usual size. The thymus body still persists and is proportionately as large in size as in the child. The tissue seems to be of the same structure as is found in the infant.

"The lymph nodes of the cervical and bronchial chains are moderately enlarged and pigmented.

"The diaphragm is relaxed, it presents no abnormality in texture or thickness, and the smooth muscle tissue making it up seems to be perfectly normal.

"The liver is small and somewhat irregular in shape. Its structure is normal.

"The spleen is enlarged to about three times its usual size. Its tissue is deep mahogany in color, firm and congested. The Malpighian bodies are apparent to the unaided eye, and the connective tissue of its septa seems to be somewhat increased. There are two spherical supernumerary splenic nodules, each 2 cm. in diameter, near the hilus of the organ. Weight of spleen, six ounces.

"The omentum and mesentery are scant in adipose. The mesentery lymph nodes are moderately enlarged, and are very firm in consistence, apparently from fibroid increase.

"The stomach is small. It contains 200 c.c. of normal appearing chyme. The mucous membrane seems to be natural, and there is no apparent disease of the muscle coats.

"The duodenum, jejunum, and ileum are entirely natural. The amount of fecal content is normal.

"The vermiform appendix is folded into a small coil and is bound to the posterior surface of the caput coli by old bands of adhesion. There are no evidences of acute inflammatory process.

"The large intestine is normal.[1]

"The pancreas is large; it is very firm, light in color, and of apparently normal structure.

"The adrenal bodies are small, the cortex is light yellow in color, and the medulla a deep red. There is no gross lesion.

"The kidneys are of about the usual size, but the left organ is considerably deformed, apparently from the pressure exerted on it by the deviation of the spinal column. The markings are fairly distinct. The capsules are not adherent, and the organs are quite natural in appearance save for a general but moderate congestion of the bloodvessels. United weight of kidneys, six ounces.

"The ureters are normal.

"The urinary bladder contains about 500 c.c. of normal urine. The mucosa of the cavity is normal, and there is no apparent disease of the muscular tissue.

"The prostate gland, urethra, testicles, and penis are all small, but are in perfectly normal condition.

"The large abdominal bloodvessels follow the deformities of the spinal column in their course. The intima of each shows a moderate amount of arterio-sclerosis, the process being less apparent in the smaller trunks.

"The skullcap is thin and quite deeply arched, though the fossæ on both sides are rather shallow, the arching being, however, somewhat more free on the left side. The configuration of the base of the cranium is normal, and it presents no deformity.

"The dural sinuses contain a small quantity of dark, partly clotted blood.

"The dura is normal. The pia-arachnoid is somewhat congested, but is not thickened and not adherent.

"The brain is of good size, is fairly symmetrical and its tissue is firm. The bloodvessels of the base are in normal condition, and those throughout the brain tissue are but moderately congested. The convolutions of the cerebrum are not particularly abundant, but they are quite typical, symmetrical, well formed, and ample, while the sulci are moderately deep. The cortical layer of gray matter is thick and regular. No gross lesion is present in any part of the encephalon.

"The pituitary gland is of usual size and apparently of normal structure.

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[1] Muscular alterations in the coats of the intestinal tract were especially sought for but the findings were entirely negative.

"The membranes of the spinal cord are negative.

"The posterior root ganglia are normal to the unaided eye; they are large and firm, but not abnormally so.

"On inspection, and on section, the various levels of the spinal cord seem to be normal; it is not abnormally firm, and the appearance of the white and gray matter to the unaided eye shows no peculiarity, and the differentiation is normally distinct.

"Examination of many of the peripheral nerve trunks from various parts of the body showed no gross abnormality in any, and the amount of perineural fat seemed in each case to be neither increased nor diminished.

"The inguinal lymph nodes are considerably enlarged, the enlargement being apparently of a fibroid character.

"No lesion of the smooth involuntary muscles in any part of the body was found.

"Nearly all the voluntary muscles showed fibroid substitution to a greater or less degree, varying greatly in amount but apparently always of the same character."

The following muscles were especially examined:

"The psoas muscles show an extensive fibrosis.

"The muscles of the back are universally of small volume, and all show extensive fibroid replacement, being light in color, very firm, and inelastic. In places there is an extensive replacement with a firm fibroid yellow fat. The fibres of the latissimus dorsi can be identified in a few places, but are mostly unrecognizable. The trapezii are very extensively invaded. The rectus capitis group are perhaps somewhat less involved, but are very firm, retracted, and inelastic. Even the muscles of the scalp show extensive fibroid changes perfectly evident to the unaided eye, but the most extreme of all the lesions of the muscle tissue is to be found in the muscles of the calves where the tissue cannot be recognized as muscle, being wholly transformed into a diffuse solid mass of firm yellowish-white tissue, apparently made up of mingled areolar tissue and fat, and in which the substituted muscle blends so completely with the structure of the tendons that it is impossible to say where muscle leaves off and where tendon begins. This tissue is of almost wood-like density. All the tendons and fasciæ of this region are much contracted.

"Cause of Death: Bronchopneumonia and fibroid myocarditis, complicated by progressive atrophy and fibrosis of the voluntary skeletal muscles."

As the tissues were removed from the body they were immediately placed in various hardening fluids. After they had become sufficiently fixed and hardened they were placed in 80 per cent. alcohol for preservation. The microscopical study was begun about five months after the time of death.[1]

These examinations were conducted with care and in great detail; as the findings were, however, largely negative they will not be given in full, but only the points of greatest importance will be considered.

The most pronounced changes of the voluntary skeletal muscles were found in the muscles of the calves. Sections of the soleus and of the gastrocnemii showed an almost complete substitution of muscle elements by a firm, dense growth of areolar connective tissue, everywhere of an adult form and with no evidences of recent cell growth or fibre production. In places the areolar tissue had become transformed into a very dense variety of adipose, characterized by the small size of the fat cells and the relatively great amount of large and densely arranged connective tissue fibres. Occasionally remnants of voluntary muscle fibres were found, but they were rare, very small, usually wholly without nuclei, and cross-striation was indistinct or absent.

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[1] We are indebted to Dr. Isador Unger, U. S. A., for the preparations of the tissues of this case.

Sections of the right psoas muscle showed similar conditions qualitatively, but here muscle fibres were much more abundant and more natural in appearance. The hyperplastic areolar connective tissue was of the same type as that found in the calf muscles, and there were also no evidences of recent connective tissue proliferation. Of the muscle fibres that remained few could be called natural; most of them were either larger or smaller than the normal, varying from small to very large, while other fibres were contracted at one point and expanded at another. Cross-striation was evident in most fibres, both large and small, and some showed this feature even more plainly than normal. Many of the cells enclosed a fine brown pigment, and in such cases there was generally more or less granular disintegration of the sarcoplasm with a corresponding indistinctness of cross-striation. Still other fibres showed the sarcoplasm mostly transformed into large fat-containing globules which were still invested by sarcolemma. Nuclei were present in most of the cells, and when present they were usually in greater number than normal and were to be seen in rows of from three to eight, just beneath the sarcolemma or extending deep into the sarcoplasm. This was especially shown in those cells which presented the more advanced stages of degeneration without fatty disintegration. Some of the supernumerary nuclei exhibited karyokinetic-like figures; usually these were atypical, and not true mitotic figures. These evidences of progressing nuclear multiplication were much less frequent than is generally found in cases of acute or progressive muscular atrophy.

The changes in all the other voluntary muscles were of a precisely similar character, varying only in the extent of the alterations. Next to the calf muscles the pectoral groups seemed most involved, though here the amount of connective tissue hyperplasia seemed to be proportionately less as compared to the muscular atrophy. The lesions were least marked in the occipital muscles, where the amount of connective tissue hyperplasia was less and the degenerative manifestations of the muscle fibres not so far advanced. Complete degeneration of the sarcoplasm was rare in these muscles, but nuclear proliferation and hypertrophic fibres were frequent. Karyokinetic-like figures were common in the chromatin of the cell nuclei, much more so than in any of the other muscles. While the atrophic changes in the fibres of these muscles were less advanced, yet no evidences of active proliferation of the cells of the connective tissue could be made out. In a few places there were collections of small round cells, situated in the region of arterioles or capillaries where they probably represented a certain degree of true inflammatory process.

Examination of the various distributions of smooth muscle tissue failed to show any evidences of degeneration or of hyperplasia of the connective tissue forming its framework, beyond a certain small amount of proliferation of the connective tissue surrounding the bloodvessels, which was found to be a general condition throughout all the tissues. Of the involuntary muscles so examined the chief were the diaphragm, the muscular tunics of the urinary bladder, of the stomach and intestines, and the muscularis of the medium and small sized arteries.

Microscopical examination of the heart muscle showed a much less degree of interstitial increase than the gross appearances led one to expect. The wall of the left ventricle exhibited a moderate augmentation of interstitium, the hyperplastic tissue being entirely of an adult type and being most abundant about the vessels. The papillary muscles showed proportionately a much greater interstitial increase. The cardiac muscle cells were found everywhere to be in a very natural condition, and, notwithstanding the apparent degeneration noted in the gross examination, there was no atrophy of the cells, no abnormal pigmentation, and no evidences of abnormal nuclear activities.

Sections of the lung taken from the pneumonic areas showed the ordinary picture of pneumonic consolidation. Sections from the uninvolved portions showed a moderate degree of emphysema, a general congestion of the capillaries, and a considerable anthracotic deposit in the lymph spaces about the air sacs. The larger vessels of the lung tissue showed an increase of the perivascular interstitium, but without any evidences of a recent process. Where the sections included small bronchi, their mucosa was found considerably congested.

Sections of the persistent thymus body demonstrated it to be made up of diffuse adenoid tissue with occasional spheres of condensation. Hassalls' corpuscles were rather less numerous than is usually the case as found in early childhood.

Sections of the thyroid gland showed no deviation from the normal.

Examination of sections of the pituitary body showed acidophylic cells numerous in the glandular portion, but no distinct lesion was found in either glandular or neural lobe.

The vessels of the adrenal bodies were found considerably engorged, and there was a moderate increase in the connective tissue framework of the glands. Examination showed no abnormality of the parenchyma.

Examination of the liver demonstrated a considerable general dilatation of the portal capillaries with congestion. There was a moderate degree of connective tissue increase in the capsule of Glisson, which was, however, devoid of all evidences of recent proliferation. Some of the liver cells contained more than the usual amount of pigment, but the fat content of the liver cells was not above the normal. The hepatic parenchyma may be said to have been practically in a natural condition.

Sections of the spleen showed a considerable degree of congestion, especially of the blood spaces. There was a general thickening of the capsule and of the septa. The Malpighian nodules were well differentiated and normally abundant. There was a large deposit of coarse, black pigment in the cytoplasm of the liver cells, free in the tissue, and distributed throughout the capsule and septa diffusely and in the connective tissue cells.

There was also an extensive anthracotic pigmentation of the lymph nodes of the neck, and to a lesser degree the same was present in the nodes of the mesentery and of the abdominal chains. The connective tissue increase in the lymph nodes was very small, and the moderate hypertrophy of the bodies seems to have been due to congestion and to pigmentation.

The pancreas was found normal, save for a slight increase in the amount of connective tissue.

The stomach and intestine showed nothing abnormal. These sections were examined particularly for alterations in the smooth muscle.

Sections of the kidney showed a considerable increase in the amount of connective tissue, the hyperplastic tissue being found both in the adult and in the actively proliferating forms, though areas showing recent growth were found only occasionally, the chief hypertrophy being in the adult form. There was a moderate general congestion of the vessels. The parenchyma in places showed a few granular and degenerated cells, but was as nearly normal as can be found in the adult human kidney under ordinary conditions.

Sections of the urinary bladder showed no abnormality.

The bloodvessels as found through the various tissues universally showed an increase in the amount of connective tissue surrounding them and uniting them to the adjacent structure. Few exhibited subendothelial hyperplasia to any considerable degree, and the inner coat of the intima was found almost always in a normal condition. No areas of perivascular infiltration were found, except as noted in the occipital muscles, and even in the sections of the extensively diseased muscles the blood channels seemed to be in a comparatively normal condition. No evidences of new vessel formation were found, and apparently the connective hyperplasia in the diseased muscles took place, largely independent of any marked vascular alterations.

Numerous peripheral nerves were examined, both in sections of the diseased muscles and as separate trunks, especially prepared to show fibre degeneration if that lesion were present. No fibres were found which showed degeneration of appreciable extent as demonstrated by the methods utilized (Müller's fluid fixation with Pal-Weigert staining; Marchi's fixation; alcohol and formalin hardening with hæmatoxylin and eosin, and Van Gieson's stains). Some of the larger trunks, as the crurals and sciatics, showed a considerable increase in the amount of endoneurium, but close observation showed this hyperplasia to be clearly of a perivascular type, originating about the small arterioles of the trunk. Sections of the atrophied muscles, which included nerve trunks, showed a perceptibly less amount of connective tissue hyperplasia in the make-up of the nerves than in the surrounding tissue.

Sections of the cœliac sympathetic ganglia fixed in alcohol and stained after the method of Nissl showed absolutely no changes which could be looked upon as degenerative, although occasionally a few cells did show more than the ordinary amount of brown pigment deposited in the cytoplasm.

Unfortunately, only a few posterior root ganglia were properly preserved for study by the Nissl method. Those which were so fixed universally showed identical lesions. These lesions consisted in a shrinkage of the ganglion cells, in many cases similar to that produced occasionally by fixing agents, but here the irregular perilymphatic spaces enclosing the shrunken cells were found filled in with the proliferating capsular cells. This would seem to indicate that cell shrinkage had taken place long before death, and that it was distinctly a pathological process. By far the greater number of ganglion cells showed a natural condition of the Nissl bodies, but occasional cells, especially the shrunken ones, were found in which an almost complete chromotolysis was present; chromolitic changes of moderate degree were still more frequently found. Chromophylia was present in a few instances, and was usually peripheral, rarely involving the entire cell cytoplasm. Nuclear changes were wholly wanting. The amount of coarse, brown pigment normally present in these ganglion cells seemed to be augmented in a few cases, and an identical pigment was occasionally found free in the stroma of the ganglion in more than natural amounts. Apparently the connective tissue stroma of the ganglia had been considerably increased, but there were no indications that this process was still advancing.

The histological examination of the spinal cord was thoroughly made, each separate segment being studied, usually by several methods, in order that different types of tract or cellular degenerations might be sought for.

The connective tissue throughout the entire cord was found to be increased, the hyperplasia in each part being strictly of a perivascular origin and of but a moderate degree. The bloodvessels of the cord were universally congested, but this congestion was apparently of a hypostatic nature. There were no indications of an inflammatory process in any part, except in the perivascular increase of connective tissue, which was obviously of a chronic character and probably but a localized manifestation of the general process.

Degenerated tracts were absent in every part of the cord. This conclusion was reached after careful study, utilizing the stain of Pal-Weigert and corroborating these findings by Marchi's method. Occasional isolated degenerated fibres were found (if we may depend absolutely on the methods employed), and these were usually in the columns of Gall or Burdach, but nothing in the nature of a systemic degeneration was indicated in any level.

Morphological changes in the ganglion cells of the spinal cord were entirely absent, and sections stained with Nissl blue demonstrated that the cytoplasmic and nuclear structure of the ganglion cells, in so far as can be determined by this method, were also for the greater part normal. Occasional ganglion cells presenting different types of degenerations as demonstrated by this method were, however, found, and it is necessary that these be considered in more or less detail.

In the cervical region the ganglion cells of the anterior horns showed in a few instances a slight nuclear eccentricity; the most common chromatophilic change in the cells of this region was a clumping of the chromatic substance into several larger and darker staining bodies while the intervening network and the remaining plaques, though they could be seen, refused the stain to a more or less degree, apparently because these chromatic elements were very finely divided. Cells were found very rarely in which there was no apparent reaction to the dye; usually, however, plaques could be faintly seen even in these cells. The dendrites universally retained their response to the stain, though in some instances the chromatic bodies seemed to have been broken up into very finely divided granules. The posterior horn cells showed degenerative alterations with equal rarity, and where change was noted it usually consisted of a finely granular disintegration of the plaques, which resulted in a more or less diffuse staining of the cytoplasm. This was limited to no particular group or variety of cells. Occasionally the achromatic elements stained to a slight degree. No nuclear changes were noted in these cells.

In the dorsal portion of the cord peripheral chromotolysis was infrequent, but the most common alteration was a perinuclear chromotolysis with a clumping of the chromatic substance in the peripheral portions of the cytoplasm. In those cells where the chromatic substance was more or less clumped the intervening unstained plaques were frequently made up of very finely divided chromatic granules. The network in the faintly stained archochromes was always very evident, even though it had refused the characteristic stain. Nearly all of the cells which showed these degenerative alterations still showed a normal arrangement of the chromatic elements of the dendrites. Eccentricity of the nucleus was found much more commonly in the dorsal cord than in the cervical segments. Not infrequently the cells which showed perinuclear chromotolysis presented a more or less marked nuclear chromotolysis as well, in which case the outlines of the nucleus blended very closely with the net of the cytoplasm. Alterations in the cells of the posterior horns were more infrequent than in the anterior horn cells.

In the lumbar cord chromolitic changes were still more rare. The most common lesion consisted in a finely granular subdivision of the plaques with a corresponding loss of staining affinity; usually this process did not involve the entire cytoplasm. Perinuclear chromotolysis was much less frequent than in the dorsal segments. A few of the lumbar cells showed an unusual amount of brown pigment collected about the nucleus.

As the brain had been hardened for the purpose of tract study, the ganglion cells of those centres could not be studied by the more recent methods. It seems very improbable that any lesion would have been found had the study been made.

The chief lesions which bear on the general condition may be summarized as follows:

Extensive atrophy, which affected nearly all the voluntary skeletal muscles, and was confined to these muscles.

Production of diffuse areolar connective tissue and adipose tissue which replaced the substance of the atrophied muscle.

Slight general perivascular connective tissue hyperplasia.

Moderate interstitial myocarditis.

Extensive degenerative changes in a few of the cells of the posterior root ganglia.

Rare and irregular types of cytoplasmic alterations without morphological change in the ganglion cells of the spinal cord.

1. Atrophy of voluntary muscles seems to have affected nearly all distributions of this tissue, though in markedly variable degree. Both history and pathological examination indicate that this process first began or was at least most rapid in the muscles of the calves.

As to the character of this process, in so far as can be determined by histological examination, it differs in no way from the atrophies which result in many widely different conditions, as from section of nerve trunks, disease of the descending tracts, or even from injuries affecting the muscle tissue direct. It is highly improbable that there are any specific modes by which voluntary muscle fibres degenerate, as has been intimated by some authors.

The process may differ in rapidity or location, but follows on certain well-defined lines, and, as in Wallerian degeneration, is probably wholly unaffected by its etiology, excepting in degree and in reparative efforts. Everything points to a slow progression of the proces,s which was doubtless inaugurated in but a limited distribution of the tissue, subsequently affecting all voluntary striated muscle.

That the atrophy of the muscle fibres preceded connective tissue hyperplasia is indicated by the conditions found in the less extensively involved muscles, where obviously the process is most recent. As an example we may cite the picture presented in the occipital muscle.

Complete absence of the changes in the smooth muscle shows that the disease process was not a general one of all muscle tissue, but was strictly localized in the voluntary muscle distribution.

Since the muscle cells of the heart showed no variation although there was a moderate interstitial increase in this viscus, we also exclude striated involuntary muscle from the involved tissues.

2. We do not look upon the connective tissue hyperplasia which took place in the process of substitution of the atrophied tissue as a primary evidence or manifestation of the disease. Everything points to the fact that the connective tissue increase was but an example of the universal function of this tissue, which by its growth fills in and replaces tissue of any form when it becomes extensively diseased or is removed.

The fact that this tissue in its growth followed natural tendencies, passing from a proliferating, semi-embryological form to a normal adult type, shows that the growth was not of itself pathological, but that it was directly allied to the normal conservative process familiarly known and described in scar formation.

3. Perivascular connective tissue hyperplasia though general was of slight degree. Of such extent it is found more commonly than not, and it certainly cannot be considered a lesion typical of the disease or produced by it. It cannot be a causative factor, or the atrophic changes found only in the skeletal muscles would also have been found in other structures.

4. Probably the moderate degree of interstitial myocarditis was associated with the connective tissue hyperplasia of the bloodvessels. Possibly it was a primary process incited by overaction of the heart or by some other and unknown cause. There is no reason why we should look upon this as in any way connected with the factors producing atrophy of the voluntary muscles.

5. We certainly must admit that the changes found in the posterior

root ganglia are of great significance. Actual morphological alterations in the cells, as well as extensive cytoplasmic changes, cannot be attributed solely to the terminal infective process or to post-mortem decomposition. It is not so clear, however, that these bear a direct relation to the atrophy of the voluntary muscles. The fact that so few of these cells were involved while the extent of the muscular atrophy was general must exclude these lesions from our consideration as primary. That secondary alterations in the ganglia might result from primary disease of the muscle seems more probable. This last is our interpretation of the degenerations, which are then secondary in nature and perhaps dependent on death or extensive disease of certain of the terminal portions of the neuron—that is, of the sensory nerve endings of the involved tissues.

A process similar to this results after amputation, especially if, as Schaffer points out, the subject be young. The cell degenerations in amputation develop very slowly, as is also the case in this condition. Undoubtedly changes in the peripheral sensory fibres precede the ganglionic degenerations. They were not observed in this case, probably because the methods now at our command are insufficient to demonstrate slight changes in single fibres of the nerve bundles.

6. We naturally look for changes in the spinal cord in processes of this nature which are progressive and so symmetrical in location as to at once attract attention to the probability of a central lesion. The majority of previous researches in this disease have, however, tended to show the absence of such lesions. It seemed, nevertheless, possible that these negative results may have been brought about by deficient or faulty methods of research, and for this reason it is important that, as newer methods of investigation are elaborated, the ground be gone over again in the hope that more perfect methods may give more certain results.

On this account our chief study in this case has been directed to the spinal cord. In summary, our results are these: There are no evidences of tract disease. The occasional isolated degenerated fibres found in the posterior columns are probably ascending central branches of the degenerated spinal ganglion cells, though it seems that most of the ganglion cells affected must have been such as have their central fibre terminate in the gray matter of the cord. Were this not the case we certainly should have found something more in the nature of a systemic degeneration of the ascending tracts. The cytoplasmic degenerations of the ganglion cells of the spinal cord are rare and of such a character as might result from post-mortem changes or from the terminal infection which was the direct cause of death. The ganglion cell changes do not appear to us sufficient or of such character as might be expected were the process a secondary one following the long standing muscular atrophy; though it seems probable that secondary degenerations of these cells might eventually result as in amputation.

For lack of a better explanation we are inclined to account for the somewhat striking chromophylic changes in certain of the cells of the dorsal segments as due to nutritive disturbances particularly affecting this portion of the cord, following the extensive and rapidly progressing curvature of that portion of the spinal column.

The chief inference to be drawn from the negative findings of this case is that the spinal cord of a patient who had suffered for over fifteen years from a distinct form of progressive muscular dystrophy did not present any evidence tending to show that the wasting of the muscles could be attributed to disease of the gray or other matter of the spinal cord. Whoever wishes to maintain Erb's theory is, of course, at liberty to do so, but it should be regarded as pure speculation. For the present there seems to be sufficient warrant to maintain the distinction between the amyotrophies and the myopathies. It is difficult, however, to account for this latter group of family afflictions unless we are satisfied simply to state that there must in these cases be some defect in the embryonal structure which does not permit of a satisfactory development of the muscular system. That the disease represents a primary affection of the muscular fibre may be taken for granted, and that the fatty degeneration of the muscular fibre is secondary to the hypertrophy and atrophy of the muscular tissue.

There are two questions which it seems wise to raise for discussion:

First, are all these cases of progressive dystrophy primary diseases of the muscular system, and may not some of them be the local expression of a universal lipomatosis? Only recently one of us had occasion to examine a boy who presented all the clinical symptoms of a pseudohypertrophy; but with the development of the pseudohypertrophy there was also developed an enormous universal lipomatosis, so that it was difficult to state whether the boy's inability to use his limbs was due to this general accumulation of fat or to a purely muscular affection. This same boy presented other distinct stigmata of degeneration, such as defective mental development and a marked chronic hydrocephalus. The occurrence of stigmata of degeneration in so many of these cases of progressive muscular dystrophy would lead one to suspect that these diseases should be classified broadly among degenerative family disorders; and possibly we may reach a better understanding of these family afflictions if we depart from the purely anatomical lines and do not regard them merely as affections of the muscular or neural systems.

Secondly, the question arises whether these muscular dystrophies are necessarily progressive. Even though they may be predestined, as it were, to develop some form of progressive wasting of the muscles, is it not possible that the tendency to progressive deterioration of the muscular system may cease either spontaneously or may be checked by treatment directed to this end? A few rather noteworthy experiences which have been accumulated during the past seventeen years have led us to be more hopeful of the future of these cases, and in these experiences—few as they are—there is sufficient encouragement to urge that in every case of progressive muscular dystrophy the possibility of great improvement by systematic exercise should be kept in mind at the very start; and there is little doubt that if earnest efforts in this direction be made at an early period, better results may be obtained than has fallen to the lot of these unfortunate patients hitherto.

The most marked instance we have to record is that of a young woman, now twenty-five years of age, who first came under our notice at the age of ten and one-half years, in September, 1886, and whose condition was reported in the *Journal of Nervous and Mental Disease* and in the *New York Medical Journal* of 1888. The history taken at that time was briefly this:

The mother was forty-seven years of age, the father ten years older; the latter has since died of sarcoma. The patient was the youngest of all the children, and was born fourteen and a half years after the next oldest sister. During the first ten months of her life there was no trouble. The parents lived next to the Brooklyn Theatre at the time of the fire, and were compelled to take the child out in that cold December night. The parents lost all their worldly possessions at that time. The mother became greatly agitated, and, nursing the child at the time, she supposed that the trouble which was developed later on was naturally due to this sad occurrence. At first the child lost flesh, and was not able to stand until she was one and a half years old. She did well until the age of six, when the first difficulty in walking was noticed, and when the mother observed that the calves were growing larger; also, that both thighs were out of proportion to the rest of the body. At that time the faradic response was absolutely normal in all the muscles and nerves of the lower extremities. In January, 1887, it was noticed that the electrical condition remained normal, and that she had great difficulty in getting up and down from a chair or in rising from the floor. The flexors of the legs and thighs were particularly weak. In 1888 it was noted in addition that the calves and anterior thigh muscles were much hypertrophied; that the sternal portion of the cleidomastoid was distinctly atrophied; that the hand muscles were very thin; that she assumed the characteristic position in rising from the floor, presented a waddling gait, and that both feet were in valgus position; the arms seemed lean and long; all the muscles contracted properly to the faradic current, except the interossei of the hand and the vasti in the thighs.

The patient did not present herself again for the following eleven years, and since that time has remained continuously under observation. She had developed into womanhood and became a kindergarten teacher; and although she had experienced and still does experience some difficulty in going up and down stairs, and particularly in getting in and out of cars, she has been able to perform all her duties and is practically well, though much annoyed by the size of her hips and thighs, and the circumference of her waist. She attributes much of her well-being to the sytematic exercise which she has been carrying on for years, and to the calisthenic movements which her calling necessitates her doing with children every day of her life. At present she merely exhibits some slight weakness of the orbicularis of the right side and of the deep spinal muscles. If placed on the floor and asked to rise she climbs up upon herself in typical fashion. The grasp of her hands is weak, but aside from this and the difficulty in climbing, and the slight waddling gait, she has little to complain of. Her intellectual development is surely up to the average. The size of her limbs may be inferred from the following measurements: Right thigh, 69 cm.; left thigh, 63 cm.; right calf, 36 cm.; left calf, 36½ cm.; measurement around hips, 112 cm.; waist measurement, 71 cm. (twenty-eight inches). The strength of the limbs is not in proportion to the size of the muscles, and it is fair to assume that the muscles are still in a condition of hypertrophy. There is no unusual lipomatosis, for above the waist line she is thin rather than stout. There is still evidence of a weakness and atrophy of the muscles around the shoulder girdle, the pectoralis showing slight wasting. The young woman has been encouraged to keep up muscular exercise, but not beyond the point of easy fatigue, for it is evident that any excess in this direction would be followed by atrophy. According to present indications there is no reason why the girl should not continue in good health for many years to come; and whether or not there was a spontaneous cessation of the tendency to hypertrophy and atrophy, the case has run an exceptionally favorable course, and as such is worth recording.

The second case was one which Dr. Wiener reported a number of years ago from my (Sachs') clinic.[1]

This case was exhibited before this Society some years ago. A few points of the history worth noting are that the patient at the time of the first examination, in 1893, was twenty-three years of age. 'Since May, 1892, he had been complaining of pains following upon active exercise; had experienced special difficulty in walking up and down stairs. The weakness of the muscles was first evidenced in the legs, then in the back, then in the hips, and, finally, in the shoulders and neck. The examination revealed marked atrophy of the muscles of the shoulders, back, hips, and thighs, as well as of the facial muscles. There was marked lordosis in the lower dorsal and upper lumbar region, He had loose shoulders and the typical gait of pseudohypertrophy.' A microscopical examination of a piece of muscle removed from the deltoid revealed atrophic fibres and a proliferation of the muscle nuclei; also, some cellular infiltration in the interstitial tissue. By means of systematic gymnastic exercises, which Dr. Wiener directed, a marked improvement was brought about in the patient, so that he was able to go about his occupation, and, as I understand, has become a very expert bicycle rider. In Dr. Wiener's article a special note was made that the only muscles which did not improve were those of the face, and these had not been subjected to special exercise.

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[1] Neurologisches Centralblatt, 1896, No. 9.

In clinical and private practice during the past few years other cases of pseudohypertrophy have been examined. and each and every one of them has been subjected to systematic exercise; and while it is still too early to report definitely upon them, it is at least safe to infer that the progressive deterioration of the muscular system can be checked, for a time at any rate, by active exercise. After all, the life of every part of the system is maintained by compelling it to perform, as far as possible, its natural physiological function. There is some reason to think that by this simple method much can be accomplished in the progressive myopathies. At all events, it would be a satisfaction to feel that a small number of the patients afflicted with progressive muscular disease may be rescued from the sad fate that awaits so many of them.

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THE MALARIA OF THE TROPICS.

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In the light of our recent knowledge of the subject, malaria may be defined as a specific infectious fever, characterized symptomatically by the following stages: Rigor, hyperpyrexia, and diaphoresis, occurring periodically; pathologically by certain changes in the elements composing the blood, and invariably by the presence in the blood of the plasmodium of Laveran; changes in the internal organs, and in the bone marrow.

Etiology. The predisposing causes are tropical climates, summer seasons, low marsh lands, dampness, decaying vegetable matter, and the prevalence of a certain species of mosquito—the Anopheles claviger.[1]

The exciting cause is the plasmodium of Laveran, which gains admission into the blood by the bite of the mosquito.

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[1] It is probable that several other species of mosquito act as the intermediate host.